REMARKS

Claims 1-9 were presented at the time of filing. Claims 1-6 were cancelled and rewritten and presented as new claims 10-13 in the Response to Restriction Requirement and Amendment filed November 13, 2006. Claims 7-13 are currently pending in the application with claims 11-13 withdrawn from consideration as being directed to a non-elected invention.

Rejection under 35 U.S.C. § 102

Claims 7 and 10 are rejected under 35 U.S.C. § 102(e) as being anticipated by Rapoport et al. (U.S 6,747,139.) According to the Office Action, Rapoport et al. disclose monoclonal antibodies against hTSH receptor which block binding of hTSH and autoantibodies to the receptor and Rapoport et al. also discloses the amino acid sequence of the hTSH receptor, which contains the FDSH sequence (amino acids 381-384.) From this the Office Action concludes that the antibody of Rapoport inherently has the ability to bind FDSH. Applicants disagree.

The claims are directed to monoclonal antibodies against the hTSH receptor having the ability to block binding of TSH and/or autoantibodies to the TSH receptor *and* bind to an epitope on the receptor having the amino acid sequence FDSH. Therefore, in order for the cited reference to anticipate the claimed antibody, both characteristics of the antibody must be disclosed. Rapoport does not disclose such an antibody.

An anticipation rejection requires a showing that each limitation of a claim must be found in a single reference. Addditionally, to constitute an anticipatory reference, the prior art must contain an enabling disclosure. A reference contains an enabling disclosure if a person of ordinary skill could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed

himself, and the public, in possession of the invention In re Donohue, 766 F.2d 531, 226 U.S.P. Q. 619 (Fed. Cir. 1985).

In the present case, Rapoport et al. disclose the nucleotide and amino acid sequences for human TSH receptor; disclosure of the FDSH (amino acids 381-383) sequence is inherent in the disclosure of the complete sequence of 764 amino acids. However, Rapoport does not disclose or suggest that there is any particular significance to amino acids 381-384 of the receptor sequence, the FDSH sequence.

Rapoport et al. also discloses general methodology for generating anti-hTSH receptor antibodies using the deduced amino acid sequence. For example, Rapoport et al. describes raising polyclonal antibodies using cells expressing the TSH receptor protein to immunize animals. Rapoport et al. also discloses generation of monoclonal antibodies by hybridoma technology, using "TSH receptor antigen" as the immunogen.

Without a teaching that the FDSH sequence is or is part of a significant epitope, the disclosure is not enabled with respect to an antibody directed to that epitope or to a method for generating an antibody that binds that specific epitope. Because Rapoport et al. is silent as to the significance of amino acids 381-384 of the hTSH receptor, the reference does not provide any suggestion or motivation for 1) generating an antibody specific for that sequence or 2) isolating an anti-hTSH receptor antibody that has specificity for the FDSH epitope from a polyclonal pool or for screening monoclonals to identify those that are directed to an FDSH epitope.

The Office Action incorrectly assumes that any antibody that blocks binding of TSH or autoantibodies to hTSH receptor must also bind the FDSH epitope. As of 2004, the precise location of TSH-receptor stimulating autoantibody (TSab) or TSH-receptor stimulating autoantibody (TBab) epitopes was still under debate (Minich et al. Clin Exp Immunol 136:129-136, 2004 page 129, second column). In the absence of information identifying specific binding sites on the receptor for TSH and autoantibodies, there is no way of knowing whether an antibody directed to the FDSH sequence would block

binding of TSH or autoantibodies to the receptor. Rapoport does not contain that information.

Lastly, immunization with the whole TSH receptor in either cell-bound or cell free form does not guarantee that an antibody to every epitope of that molecule will be produced. The location of the FDSH sequence in the intact, folded receptor, for example might be in the interior of the molecule as opposed to on the surface; this information was not available at the time of Rapoport et al. It is not necessarily the case, therefore, that an antibody to the FDSH molecule would be produced in response to challenge with the intact receptor.

In Applicants' view, the description of anti-TSH receptor antibodies in Rapoport constitutes a generic disclosure of methods for generating anti-hTSH receptor antibodies, but does not place the skilled artisan in possession of an antibody that specifically recognizes/binds the FDSH epitope as claimed by Applicants. Therefore, Rapoport cannot anticipate the claimed monoclonal antibody. Withdrawal of the rejection under 35 U.S.C. §102 is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 7-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rapaport et al. (U.S. Patent No. 6,747,139), in view of Vanderbark et al. (U.S. Patent No. 5,614,192). According to the Office Action, it would have been obvious to one of skill in the art to humanize the antibodies of Rapoport by using the method of Vandenbark.

As discussed above, Rapoport et al. does not teach an anti-hTSH receptor antibody that binds to the FDSH (amino acids 381-384) amino acid sequence of the hTSH receptor.

Vandenbark discloses T-cell receptor peptides and antibodies directed thereto. The teachings of Vandenbark do not compensate for the deficiencies in the teachings of Rapoport et al., because, like Rapoport et al., Vandenbark fails to teach the significance of the FDSH sequence of the hTSH receptor and an antibody directed thereto. In the absence of such teaching, there is no motivation to make the claimed antibody, let alone humanize it. Accordingly, the combination of teachings of Rapoport and Vandenbark do not result in Applicants' claimed monoclonal antibodies.

In view of the above arguments, withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

Kathy Smith Dias
Attorney for Applicants
Reg. No. 41,707

Dated: March 19, 2008

Address for Correspondence:
Kathy Smith Dias
HESLIN ROTHENBERG FARLEY & MESITI P.C.
5 Columbia Circle
Albany, New York 12203-5160
Telephone: (518) 452-5600
Facsimile: (518) 452-5579